Synthesis of Some Uridine and Cytidine Derivatives

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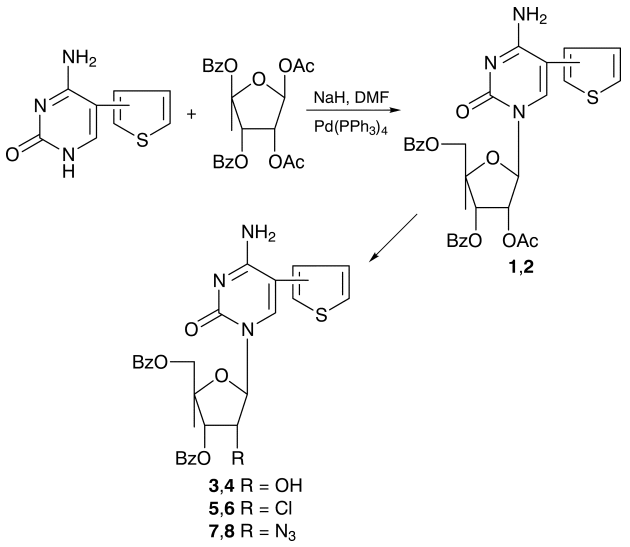
Some modified nucleosides were prepared from 5,6-disubstituted uridine, 5-substituted cytidine and cytidine by nucleophilic substitution reactions in alkaline or neutral medium; preliminary antibacterial activities of the synthesized compounds have been measured.

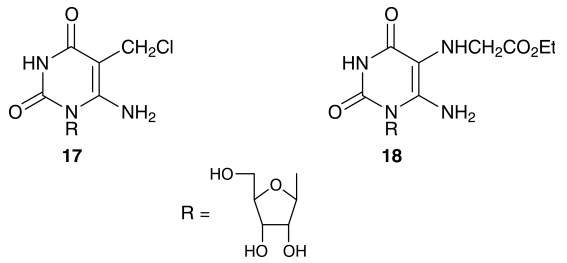
5-(2″-Thienyl) and (3″-thienyl)cytosine derivatives were prepared as shown in Scheme 1. The iodination of cytosine then the trimethyl silylation reaction and the concentration with tributyl-2- and 3-thienyl ring were performed as before.[15–19] The coupling of both of the silylated derivatives, 5-(2″-thienyl) and (3″-thienyl)cytosine, with 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-*β*-D-ribofuranoside was carried out in *N*,*N*-dimethylformamide to give compounds **3** and **4** in high yield. The latter compounds were reacted with thionyl chloride in acetonitrile at 75 °C to give the chloro derivatives **5** and **6**. Both **3** and **4** were converted into the corresponding 2′-azido compounds **7** and **8**, respectively, by the reaction with diphenyl phosphorazidate, and diethyl azodicarboxylate and triphenylphosphine, in THF.



Scheme 1

Advantage was taken of the facile formation of 6-azidouridine from uridine and of the ease with which the 6-azido group undergoes nucleophilic substitution to prepare 6-amino-5-hydroxymethyluridine (**17**) from 5-hydroxymethyluridine, and 6-amino-5-ethoxycarbonylmethyluridine (**18**) from 5-bromouridine.

Mention should be made that compound **17** was prepared by reaction of 5-hydroxymethyluridine with sodium to form



Scheme 2

5-hydroxymethyl-6-azidouridine (**11**) which was reacted with ammonia solution to give 6-amino-5-hydroxymethyl-aminouridine.

The latter compound reacted with HCl in dioxane to give **17**.

On the other hand, compound **18** was prepared by the reaction of bromouridine with ethyl glycine ester. The resulting product reacted with sodium azide to give the 6-azido derivative which reacted with ammonium hydroxide solution to afford **18**.

Techniques used: IR, ^{1}H NMR and mass spectrometry

References: 21

Schemes: 2

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References cited in this synopsis

15 D. Peters, A. B. HörnFeldt and S. J. Gronowitz, *Heterocycl. Chem.*, 1991, **28**, 1613.
16 K. A. Watanabe, T.-L. Su, R. S. Klein, C. K. Chu, A. Matsuda, M. W. Chun, C. Lopez and J. J. Fox, *J. Med. Chem.*, 1983, **26**, 152.
17 D. Peters, A-B. Hörnfeldt, S. Gronowitz and N. G. Johansson, *Nucleosides Nucleotides*, 1992, **11**, 115.
18 M. Krecmerova, H. Hrebabecky, M. Masojidkov and A. Holly, *Collect. Czech. Chem. Commun.*, 1995, **61**, 458.
19 A. Matsuda, J. Yasuoka, T. Sasaki and T. Ueda, *J. Med. Chem.*, 1991, **34**, 999.